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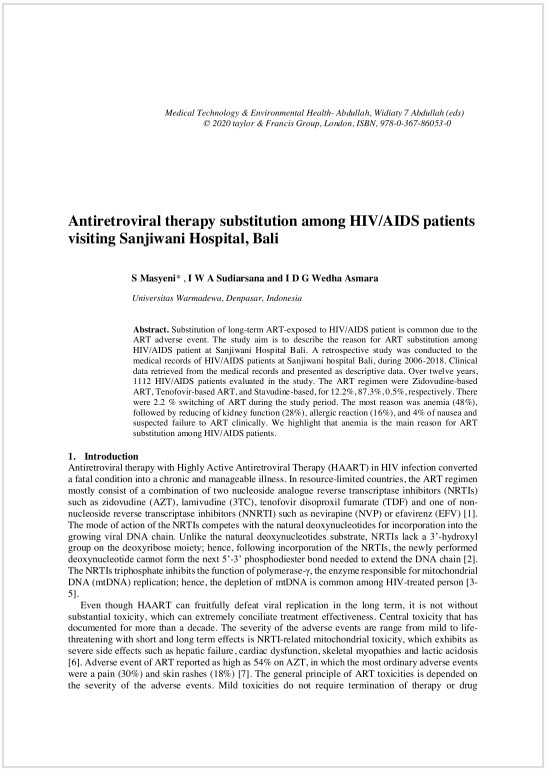

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Antiretroviral therapy substitution among HIV/AIDS patients visiting Sanjiwani Hospital, Bali

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Abstract. Substitution of long-term ART-exposed to HIV/AIDS patient is common due to the ART adverse event. The study aim is to describe the reason for ART substitution among HIV/AIDS patient at Sanjiwani Hospital Bali. A retrospective study was conducted to the medical records of HIV/AIDS patients at Sanjiwani hospital Bali, during 2006-2018. Clinical data retrieved from the medical records and presented as descriptive data. Over twelve years, 1112 HIV/AIDS patients evaluated in the study. The ART regimen were Zidovudine-based ART, Tenofovir-based ART, and Stavudine-based, for 12.2%, 87.3%, 0.5%, respectively. There were 2.2 % switching of ART during the study period. The most reason was anemia (48%), followed by reducing of kidney function (28%), allergic reaction (16%), and 4% of nausea and suspected failure to ART clinically. We highlight that anemia is the main reason for ART substitution among HIV/AIDS patients.

1. Introduction

Antiretroviral therapy with Highly Active Antiretroviral Therapy (HAART) in HIV infection converted a fatal condition into a chronic and manageable illness. In resource-limited countries, the ART regimen mostly consist of a combination of two nucleoside analogue reverse transcriptase inhibitors (NRTIs) such as zidovudine (AZT), lamivudine (3TC), tenofovir disoproxil fumarate (TDF) and one of non-nucleoside reverse transcriptase inhibitors (NNRTI) such as nevirapine (NVP) or efavirenz (EFV) [1]. The mode of action of the NRTIs competes with the natural deoxynucleotides for incorporation into the growing viral DNA chain. Unlike the natural deoxynucleotides substrate, NRTIs lack a 3'-hydroxyl group on the deoxyribose moiety; hence, following incorporation of the NRTIs, the newly performed deoxynucleotide cannot form the next 5'-3' phosphodiester bond needed to extend the DNA chain [2]. The NRTIs triphosphate inhibits the function of polymerase-γ, the enzyme responsible for mitochondrial DNA (mtDNA) replication; hence, the depletion of mtDNA is common among HIV-treated person [3-5].

Even though HAART can fruitfully defeat viral replication in the long term, it is not without substantial toxicity, which can extremely conciliate treatment effectiveness. Central toxicity that has documented for more than a decade. The severity of the adverse events are range from mild to life-threatening with short and long term effects is NRTI-related mitochondrial toxicity, which exhibits as severe side effects such as hepatic failure, cardiac dysfunction, skeletal myopathies and lactic acidosis [6]. Adverse event of ART reported as high as 54% on AZT, in which the most ordinary adverse events were a pain (30%) and skin rashes (18%) [7]. The general principle of ART toxicities is depended on the severity of the adverse events. Mild toxicities do not require termination of therapy or drug

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substitution, and symptomatic management may give (e.g., antihistamines for a mild rash). Moderate or severe toxicities may require substitution with a drug in the same ART class but with a different toxicity profile, or with a drug in a different class, but do not require discontinuation of all ART. Severe life-threatening toxicities need cessation of all ARV drugs, and the commencement of proper supportive therapy until the patient alleviated, and the toxicity is committed. Substitution of long-term ART-exposed to HIV/AIDS patients are common due to the ART adverse event [7].

However, only a little information is known about ART adverse events in many HIV programs in the public health sector of developing countries. The study aim is to describe the reason for ART substitution among HIV/AIDS patient at Sanjiwani Hospital Bali.

2. Methods

The current study was a hospital-based retrospective observational study conducted at HIV care clinics in Gianyar Bali from 2006- 2018. The hospital has an HIV clinic, staffed with health professionals trained in ART treatment and adherence counseling services. Clinical data retrieved from the medical records and presented as descriptive data. The reasons for substitution retrieved from the medical record. A data-gathering format used to collect data on the demographic settings, the starting and changing regimens, the period of the initial therapy, CD4 count, and World Health Organization (WHO) stage of the disease, and reasons for regimen substitution. Adverse drug reactions (ADR) is defined as the occurrence of adverse events such as diarrhea, nausea, vomiting, anemia, rash, fatigue, peripheral neuropathy, lipodystrophy, metabolic disturbances or any other related to HAART. Substitution defined as single or triple drug change due to side effects and initiating another drug of the same class and or another category.

3. Results

A total of 1.094 medical records of HIV-infected at Sanjiwani Hospital assessed in the study. Female patients account in the minority, as high as 29% and 7(0.6%) of the female participants was pregnant. The median age of the participants is 32.5 (IQR 13) years old. Total CD4+ ≤100 cell/mm^3, CD4+ 101-200 cell/mm^3, CD4+ 201-350 cell/mm^3, CD4+ 351-499 cell/mm^3, and CD4+ ≥ 500 cell/ml accounting for 347 (31.7%), 139 (12.7%), 173 (15.8%) and 37 (93.4%) respectively.

Table 1. Characteristic of the participants (N=1094)

Variable	Frequency	Percentage (%)
Gender		
Male	777	71
Age		
18-30	470	42.96
31-40	382	34.92
41-50	166	15.17
51-60	58	5.31
61-70	17	1.55
>70	1	0.09
Initial Body Weight		
Median (IQR)	55 (12)	
Initial CD4 (IQR)	136 (246)	
HIV stage (WHO)		
Stage 1	115	10.5
Stage 2	109	10
Stage 3	431	39.4
Stage 4	439	40.1

The first line original ART consists of stavudine-based, tenofovir-based, and zidovudine-based ART. The stavudine ART in combination with lamivudine and nevirapine or efavirenz, as well as the combination of TDF and ZDV. Characteristic of the participants presented in table 1. A majority of the patients were on the combination of tenofovir+lamivudine+efavirenz, the fixed-dose combination ART (738/67.5%).

Total switching of the ART found in 26 (2.37%) patients. Ten of 26 (38.46) switching was on ZDV-based as the original ART. Adverse events of ART found in 22 (2.01%) patients. Type of adverse events is anemia 4 (18.18%), itchy 10 (45.45%), a decrease of kidney function seven (31.82) and gastrointestinal problem 1 (4.55%). The adverse effect anemia and itchy mostly relate to the combination of ZDV+3TC+NPV and another first-line ART, TDF+3TC+EFV is the most ART of choice substitute the previous ART. On the other hand, reducing kidney function may relate to TDF-based ART and change to ZDV-based ART. Fifty percent of the switching occurs in the first year of treatment.

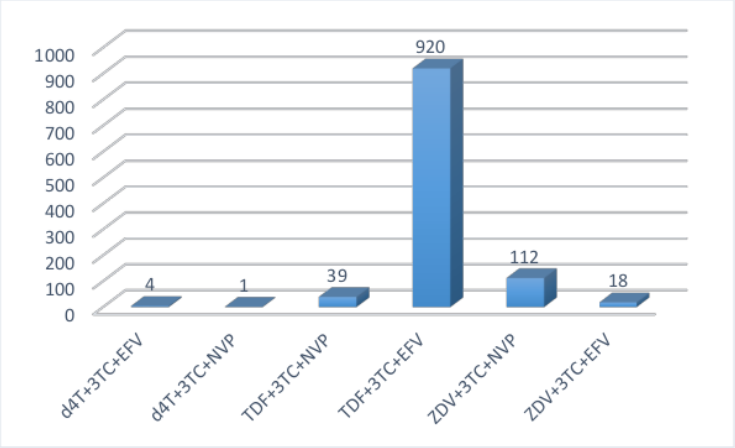

Figure 1. Profile of ART among the HIV-infected patients

The switching to second-line ART found in four (0.36%) of the patients due to the suspicion of treatment failure whether clinical failure 33.3% and immunological failure 66.7%. The ART of choice for switching due to treatment failure is boosted lopinavir/ritonavir in combination with TDF+3TC.

4. Discussion

Acquired immunodeficiency syndrome (AIDS) caused by the human immunodeficiency virus (HIV) is a major global health problem [8]. There are several studies of HIV infection in Bali due to subtype characteristic [9], toxicity [5], adherence [10], and co-infection [11] which reflect the epidemic of HIV infection in Bali. The main reasons for treatment conversion might be due to, adverse events, poor adherence, a desire for pregnancy, treatment failure [12]. The high finding of male patients who need ART substitution in the current study is supported by another study where they found as high as 53.7%.

The median CD4 of the study participants is 136 cell/mm^3. In contrast with the finding of the previous study where they found the median CD4 of the patients was 201 cell/mm^3 [13]. The discrepancy may associate with the social demographics of the countries affect the immune status of the patients. The study found toxicity (88%) as the most reason to change the ART regimen. A concordance finding reported by other study that found as high as 72.73% ART changing due to toxicity [14]. This similar finding may due to the HIV sub-type is HIV-1, but we do not assess the genetic diversity of the patients.

The most common primary ART in the current study is TDF-based regimen, which is in contrast with previous study Zidovudine-based ART where the primary ART was ZDV-based ART [15]. In Indonesia, the availability of TDF since 2014 become the ART of choice due to merely way to replace others ART of choice. Likewise, the ZDV adverse events such as anemia may associate with the common ART to switch to another regimen in this study. Another study found ART substitution most commonly found due to NVP toxicities [16]. This study found toxicity due to NVP although in the minority, that may explain with the most ART use at the hospital is TDF+3TC+EFV.

5. Conclusion

We highlight the most ART substitution in the study due to ART toxicities, instead of treatment failure. This finding may help the physician in monitoring the ART adverse event in improving the services for the patient's convenience.

6. Acknowledgment

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7. Conflict of interest

The authors declare no conflict of interest

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